REMARKS

Claims 15-16 and 18-24 are pending in the present application.

I. The Rejection of Claims 15-16, 18-24 Under § 112, 1st Paragraph Is Rebutted by the Clear Content of the Specification.

The previous Office Action dated February 25, 2004 correctly noted that the present specification discloses the use of amniotic fluid as the source of the body fluid used in the method of the invention. There does not appear to be room for doubt that the specification discloses amniotic fluid as the "body fluid employed to produce the data provided in the specification.." The following portions of the specification clarify this point:

> On page 1, lines 1-9 the title and field of the invention reads as follows:
>
> TREATMENT OF CHROMOSOMAL ABNORMALITIES IN FETUSES THROUGH A COMPREHENSIVE METABOLIC ANALYSIS OF AMNIOTIC FLUID
>
> FIELD OF THE INVENTION
>
> The present invention relates to the diagnosis of biochemical abnormalities found in a fetus. Specifically, the present invention is a comprehensive metabolic profile of an amniotic fluid specimen to diagnose and prescribe treatment for chromosomal disorders, preferably Down's Syndrome, that may be present in fetus.
>
> On page 4, line 19 through page 5, line 5 of the specification reads as follows:
>
> The present invention uses a sample of amniotic fluid to generate a comprehensive metabolic profile to diagnose chromosomal abnormalities in the fetus. The profile can be generated by several analytical techniques, and the components of the profile can be varied based on the clinical indication of interest.

For example, a procedure similar to one described by Shoemaker and Elliott can be used to screen a specimen of amniotic fluid for metabolites. Shoemaker and Elliott, *Automated screening of urine samples for carbohydrates, organic and amino acids after treatment with urease,* Journal of Chromatography, 562 (1991) 125-138, specifically incorporated herein by reference. A specimen of amniotic fluid is first obtained. For example, amniotic fluid may be taken from around the fetus during pregnancy. The specimen then is analyzed in a gas chromatograph/mass spectrophotometer (GC/MS).

On page 5, lines 17-22 of the specification read as follows:

DETAILED DESCRIPTION OF THE INVENTION

As previously discussed, a procedure similar to the procedure described by Shoemaker and Elliott may be used to screen an amniotic fluid specimen for metabolites. An amniotic fluid specimen is obtained from the fetus to be evaluated. For example, amniotic fluid may be obtained by placing a needle through the abdomen and uterine wall into the uterus and withdrawing the fluid with a syringe.

On page 17, lines 6-8 of the specification read as follows:

Mono-carbon shortage explains the finding of elevated normetanephrine in Down Syndrome (Mean = 0.039, Median = 0) compared to normal amniotic fluid (Mean = .0013, Median = 0).

On page 21, lines 1-12 of the specification (reciting an original claim) reads as follows:

WHAT IS CLAIMED IS:

1. A method of characterizing a chromosomal abnormality in a fetus by performing a comprehensive biochemical analysis of a specimen of amniotic fluid comprising:

obtaining a comprehensive profile of metabolites in the specimen of amniotic fluid,

comparing the profile with a control profile of metabolites that is representative of normal levels of metabolites,

analyzing the profile with respect to the normal profile by identifying each metabolite that has a different level when compared with the normal level of that metabolite,

generating a biochemical characterization of the abnormality, and

prescribing a biochemical treatment for each metabolite that has a different level when compared with the normal level of that metabolite.

On page 22, lines 8-19 of the specification read as follows:

7. A method of performing a comprehensive biochemical analysis of a specimen of amniotic fluid in order to characterize a chromosomal abnormality in a fetus comprising:

obtaining a comprehensive profile of metabolites in the specimen of amniotic fluid,

comparing the profile with a control profile of metabolites that is representative of normal levels of the reported metabolites,

analyzing the profile with respect to the normal profile by identifying each metabolite that has a different level when compared with the normal level of that metabolite,

inferring an activity level for an enzyme that corresponds to the identified metabolite,

inferring a cofactor level based on the activity level for the enzyme,

generating a global biochemical characterization of the abnormality, and

prescribing a biochemical treatment for each metabolite that has a different level when compared with the normal levels.

These portions of the present specification expressly identify amniotic fluid as the body fluid employed to produce the data provided in the specification. The specification shows that one may diagnose Down Syndrome from the patient's data and a comparison to a control profile wherein both types of data are obtained from the amniotic fluid.

The excerpt at p. 21, lines 6-8 expressly show the comparison of patient to control amniotic fluid. Regarding use of the specific term to describe a fetus/patient, the terminology is that used in ordinary medical practice. The Office Action questions the use of a patient's amniotic fluid, the diagnosis of a fetus and reference to the "Down Syndrome" patient. The terminology could not be used in any other way. The amniotic fluid is obviously taken from the

mother who is the "patient" at the time of the analysis and the "patient" from whom control samples are taken. This amniotic fluid provides biochemical information about the fetus, which may be analyzed, and correlated to the clinical condition of the child once born. Thus, the example in the specification is an exemplification of the claimed method that performs a diagnosis of Down Syndrome from the amniotic fluid of the fetus.

II. The Amended Claims Clarify the Use of the Pattern of Amniotic Fluid Specimen and the Analysis of Metabolite Quantities and Satisfy the Requirements of § 112, 2nd ¶ to Particularly Point Out and Distinctly Claim the Subject Matter of the Invention.

The Examiner objects to the phrase: "each metabolite pattern of the quantity of ...". This language has been revised to focus on the profile of the amniotic fluid specimen as is clearly described in the specification.

Second, the phrase "the subject of metabolites" in claim 16 has been corrected.

Finally, the objection to the phrase "pattern of the quantity of a metabolite" has been amended to specify that the method of the invention comprises an identifying and comparison step between the metabolite profile from the amniotic fluid to the control profile. The analysis of a pattern of metabolite quantities is exemplified by the comparison of the sample to the control profile as conducted in the Example of the specification.

CONCLUSION

Applicant notes absence of prior art rejections of the presently claimed method, and submits that the foregoing amendments and comments render the application in condition for allowance and respectfully requests such action accordingly.

By entry of this Amendment, Applicant respectfully submits that all of the Examiner's rejections have been overcome. Additionally, the Examiner is invited to telephone the undersigned representative if the Examiner believes that a telephonic interview would advance this case to allowance.

The Commissioner is authorized to charge Orrick Herrington & Sutcliffe's Deposit Account No. **150665** in the amount of **$490.00** for the three-month extension fee. The Commissioner is also authorized to charge any additional fees required by the filing of these papers, and to credit any overpayment to Orrick Herrington & Sutcliffe's Deposit Account No. **150665.**

Respectfully submitted,

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